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Research article

Radiological and histological findings characteristic of AIDS related Burkitt lymphoma

Yixian Luo [a], Puxuan Lu [a,*], Xiaohua Le [b], Xiaojie Luo [c]

[a] *Department of Radiology, The Third People's Hospital of Shenzhen, China*
[b] *Department of Pathology, 518112, China*
[c] *Department of Radiology, Beijing Hospital, China*

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Abstract

Objective: To explore the radiological and histological findings characteristic of AIDS related Burkitt lymphoma.
Methods: Radiological and histological data from 4 patients with AIDS related Burkitt lymphoma were retrospectively analyzed. All the 4 patients received CT scanning and MR imaging. Of the 4 patients, 3 underwent surgical removal of lymphoma and the other 1 was performed aspiration biopsy.
Results: All the 4 patients were detected with superficial lymphadenopathy, with 2 at the neck and the other 2 at the armpit. Extra-nodal invasion were found in 3 patients, of which 2 had multi-organ lesions. Their diagnoses were histologically defined to be Burkitt lymphoma.
Conclusion: AIDS-related Burkitt lymphoma is radiologically shown as lymphadenopathy and multi-organ involvement. Diffuse tumor cells with moderate sizes exist in intra- and extra-nodal tissues, characterized by stars-in-the-sky sign. Immunohistochemically, both CD10 and CD20 are positive, and the positive rate of Ki67 is almost up to 100%.

Keywords: AIDS; Lymphoma; Tomography; X-ray computed; MRI

1. Introduction

AIDS is the terminal stage of HIV infection, which destroys CD4+ T cells and disables human immunity. Therefore, it increases the risk of opportunistic infections and malignancies. Statistically, the prevalence of lymphoma in AIDS patients is about 5%–20% [1,2], only being second to that of Kaposi sarcoma. Lymphoma complicating AIDS mostly originates from B cell, and highly aggressive Burkitt lymphoma accounts for about 60%. The other cases of lymphoma are mainly moderately aggressive diffuse large B cell lymphoma (DLBCL) [3,4]. In the present study, the radiological and histological data from 4 patients with AIDS related Burkitt lymphoma were retrospectively analyzed. In combination to present literature, we intended to achieve further knowledge about this disease. And clinically, our study provided knowledge to increase the diagnostic accuracy of this disease.

2. Materials and methods

2.1. Clinical data

A total of 4 patients with AIDS complicated by Burkitt lymphoma admitted to our hospital from Jan 2009 to Jul 2014 were enrolled for the study. All the patients were male aged from 25 to 61 years. One patient experienced emaciation, anorexia and expectoration; 2 other patients were diagnosed with cervical neoplasm; and the other 1 patient showed axillary lump. Their $CD4^+$ T cell counts in blood samples were 21–407 cells/μL. The clinical data of all 4 patients was shown in Table 1.

* Corresponding author.
E-mail address: lupuxuan@126.com (P. Lu).
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Table 1
Clinical data of all the 4 patients with AIDS complicated by Burkitt lymphoma.

No.	Sex	Age	Primary site	HAART	Chemotherapy	CD4+ Counts (/μL)	Prognosis
1	M	35	Right Cervical	None	None	407	Death after 10 days
2	M	36	Left Axillary	D4T+3TC+NVP	Discharged, unknown	42	Discharged, unknown
3	M	61	Right Axillary	D4T+3TC+KLZ	Discharged, unknown	146	Discharged, unknown
4	M	25	Left Cervical	D4T+3TC+NVP	Modified R-epoch	21	Death after 6 months

2.2. Radiological examination

All the 4 patients underwent chest CT scanning. One patient received orbital and cervical CT scanning. Another 1 patient underwent upper abdominal CT scanning with contrast enhancement. And other 1 patient underwent both CT scanning and MR imaging of the brain and lumbar vertebrae.

2.3. Histological examination

Two patients were diagnosed with cervical lymphadenectomy, another one patient with axillary lymphadenectomy and the other one had axillary lymph nodes aspiration biopsy. H&E staining and immunohistochemistry were performed for pathological examination. According to the typing criteria of lymphoma proposed by WHO in 2005, all the 4 patients were diagnosed with Burkitt's lymphoma, a subtype of Non-Hodgkin's lymphoma.

3. Results

Radiologically, the 4 patients with AIDS complicated by Burkitt lymphoma were defined as having superficial lymphadenopathy. And 3 patients were revealed with extra-nodal and multi-organ invasion. The radiological findings of all 4 patients with AIDS complicated by Burkitt lymphoma were shown in Table 2.

AIDS-related Burkitt lymphoma in the 4 patients were histologically identical, specifically, diffuse tumor cells in moderate size and with uniform morphology, karyokinesis and starry-sky sign both within or out of the examined lymph nodes. Immunohistochemically, all the patients were found CD10 and CD20 positive. And the positive rate of Ki67 reached over 90%. Two patients were found positive to Bcl-6, another patient was EBER positive, and the other one was CD79 and CD43 positive. Specific histological findings were shown in Table 3 Figs. 1–4.

4. Discussion

Burkitt lymphoma is prevalent in Africa and especially common in children. About 70% of the cases show maxillofacial bones invasion and nearly 8% with marrow infiltration. The sporadic cases in Europe and America are predominantly children, with about 90% cases of abdominal invasion, and about 90% cases of marrow infiltration during the early and relapsed periods [5]. Lin et al. reported that children is the predominant population with Burkitt lymphoma in China. Cervical lymph nodes, abdomen, maxilla facial oropharynx are the top 3 vulnerable sites, with incidences of about 68.1%, 63.8% and 34.8%, respectively, while the incidence rate of marrow infiltration is about 21.9% [6]. As for AIDS-related Burkitt lymphoma, it commonly occurs in young population to invade bone marrow, lymph nodes, and gastrointestinal tract [7,8]. AIDS is the terminal stage of HIV infection, during which the CD4+ T cell count dramatically decreases to below 200/μL, indicating severe immunodeficiency. Thus, the incidences of opportunistic infection and secondary

Table 2
Radiological findings of all the 4 patients with AIDS complicated by Burkitt lymphoma.

No.	Radiological modality	Lymph nodes	Extra-node invasion
1	Cervical, Thoracic and Orbital CT	1. Right submandibular lymphadenopathy, 32 mm × 19 mm in size 2. Multi-lymphadenopathy in mediastinum	1. Multiple pleural nodules, with markedly enlargement in reexamine 9 days later 2. Focal hypoattenuating within liver 3. Localized swelling of left lateral rectus, right optic nerve enveloped by mass in posterior oculus region
2	Thoracic CT	Huge lymph node in left axils, 134 mm × 124 mm in size, with necrosis within the node	No significance in the lung and mediastinum
3	Thoracic CT	Right axillary lymphadenopathy, 32 mm × 21 mm in size	Multiple scatted nodules in bilateral lung
4	Thoracic, Upper Abdominal and Lumbar Vertebral CT, and Cerebral, Lumbar Vertebral MRI	Left cervical lymphadenopathy, 70 mm × 50 mm in size	1. General enlargement in pancreas, especially in caput pancreatis with hypoattenuating and ill-defined boundary, dilation of pancreatic duct 2. Patchy hypointensity in bilateral frontoparietal lobe (long T1 and long T2 signal in MRI) 3. L2, 4,5 vertebral body compressed change without narrowed intervertebral space 4. Spinal cord expanded from T6 to conus level with long T1 and long T2 signal

Table 3
Histological findings of 4 patients with AIDS complicated by Burkitt lymphoma.

No.	Position and operative method	Gross appearance	Cytological manifest	Immunohistochemical results
1	Right cervical lymph nodes/resection	Multi-lymphadenopathy inferoposterior to right submandibular gland; the enlarged lymph node reaches the size of 25 mm × 20 mm. The node was soft and its section is grey and taupe in color.	Intra and extra lymph nodes tissues were found diffused tumor cells with moderate size, unanimous morphology, karyokinesis and 'starry sky' phenomenon.	CD3 (−), CD20 (+), CD10 (+), Bcl-6 (+), Ki67 (about 90%+)
2	Left maxillary lymph nodes/aspiration	None	Intra and extra lymph nodes tissues were found diffused tumor cells with moderate size, unanimous morphology, karyokinesis and 'starry sky' phenomenon.	CD3 (−), CD20 (+), CD10 (+), Bcl-6 (+), Ki67(about 95%+), TdT (−), MUM-1 (−)
3	Right maxillary lymph nodes/resection	Destructed architecture of lymph node	Intra and extra lymph nodes tissues were found diffused tumor cells with unanimous morphology, karyokinesis and 'starry sky' phenomenon.	CD10 (+), CD20 (+), Ki-67 (about 90%+), EBER (+), TdT (−)
4	Left cervical lymph nodes/resection	Destructed architecture of lymph node	Intra and extra lymph nodes tissues were found diffused tumor cells with unanimous morphology, karyokinesis and 'starry sky' phenomenon.	CD3 (−), CD7 (−), CD79 (+), CD20 (+), CD10 (+), Ki-67 (about 90%+), CD43 (+), TdT (−), CD30 (−)

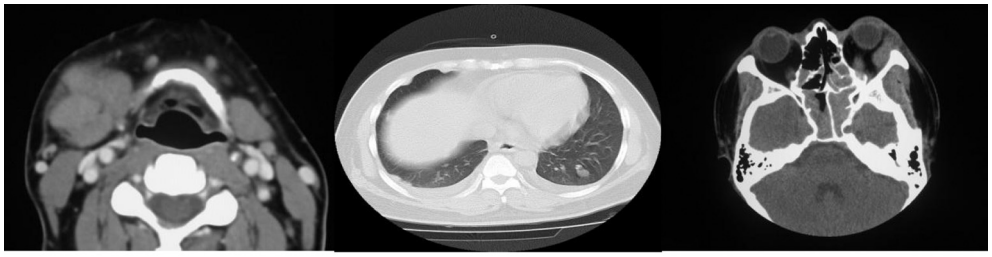

Fig. 1. A: Cervical CT scanning with no contrast showed right submandibular multi-lymphadenopathy, with a maximal size of 32 mm × 19 mm, that tended to fuse; B: Thoracic CT scanning with no contrast showed multiple pleural nodules and a nodule at the left lower lung; C: Orbital CT scanning with no contrast presented localized swelling of the left lateral rectus and that the right optic nerve was enveloped by mass at the posterior oculus region.

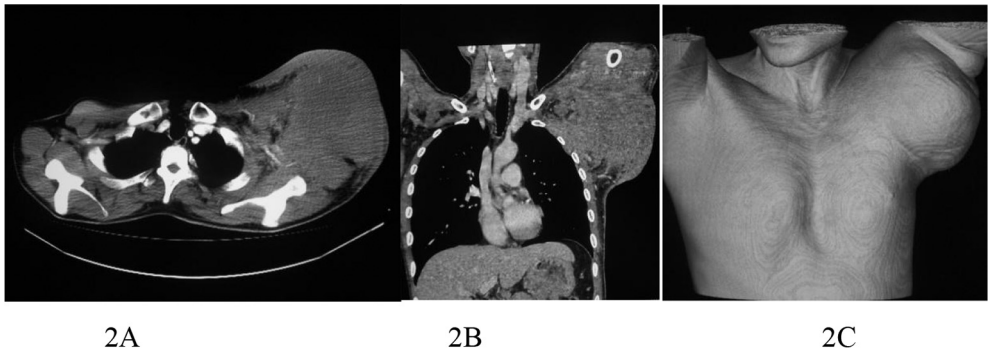

Fig. 2. A–C: Thoracic CT scanning with no contrast showed huge lymph node in left armpit in a size of 134 mm × 124 mm as well as necrosis within the node.

malignancies increase. Among malignancies associated to AIDS, the incidence of lymphoma secondary to Kaposi's sarcoma is 60 times as high as that in non-HIV-infected patients. AIDS associated lymphoma is mostly non-Hodgkin lymphoma, and the cases of Burkitt lymphoma account for about 60%. And radiological findings of AIDS associated lymphoma generally include the following two aspects.

4.1. Lymphadenopathy

Both superficial and deep (mediastinal and retroperitoneal) lymphadenopathy are radiologically demonstrated. Superficial lymphadenopathy is common in cervical, axillary and inguinal regions, with a maximal diameter of above 3 cm. Multiple enlarged lymph nodes usually have poorly defined boundaries

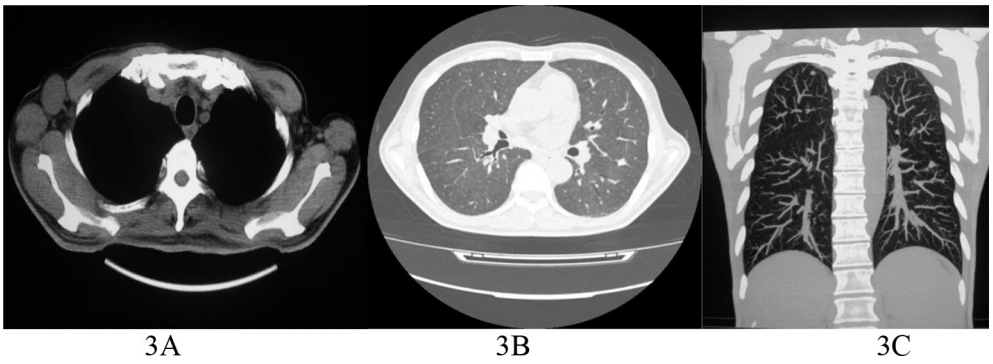

Fig. 3. A–C: Thoracic CT scanning with no contrast showed right axillary lymphadenopathy and scatted multiple nodules in both lungs.

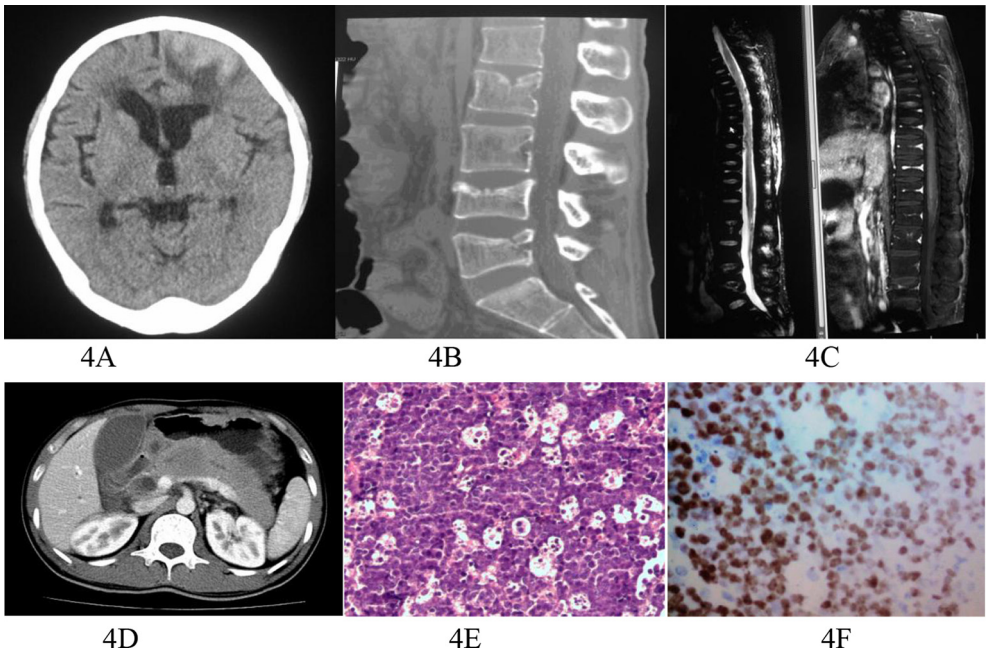

Fig. 4. A: Craniocerebral CT scanning with no contrast showed patchy hypointensity in bilateral frontoparietal lobes; B: Lumbar vertebral CT scanning with no contrast showed vertebral body to be compressed at L2, L4 & L5 with no narrowed intervertebral space; C: Thoracic and lumbar vertebral MR imaging with no contrast showed expanded spinal cord from T6 to conus level with long T1 and long T2 signal; D: Abdominal CT scanning with contrast showed general enlargement of the pancreas, especially at the caput pancreatis with hypoattenuating and poorly-defined boundary, dilation of pancreatic duct; E: H&E staining (×40) showed diffuse tumor cells with uniform morphology, karyokinesis and starry-sky sign; F: Immunohistochemistry showed CD20 positive.

[9]. All 4 patients are shown with superficial lymphadenopathy, which has a maximal diameter of 13 cm and internal necrosis. Mediastinal lymphadenopathy is also found in one patient, in consistency with previous study findings. Reactive lymphoid hyperplasia is general shown in patients with AIDS, which should be differentiated from lymphoma. The lymph nodes invaded by lymphoma are usually huge in size, with central necrosis, while those involved by reactive hyperplasia are in size of less than 3 cm. In addition, lymphoma tends to invade multiple sites and develops rapidly both in size and amount, with signs of malignancy.

4.2. High incidence of lymphoma in extra-nodal tissues

High incidence of lymphoma in extra-nodal tissues was reported to be about 98% [10]. It has been reported that the gastrointestinal tract is the most vulnerable site for its invasion, especially the ileum. Other vulnerable parts for occurrence of lymphoma in patients with AIDS also include liver, mediastinum, nervous system and skeleton [10,11]. Diffuse uneven thickening of the gastrointestinal walls and luminal narrowing are common in the cases with gastrointestinal lymphoma [12]. Hepatic lymphoma presents hilar mass with no invasion to surrounding vessels, which is known as the floating-aorta sign [13,14]. Brain lymphoma commonly arises from periventricular regions or deep white matter with multiple nodules or irregular masses, which are heterogeneous or ring-like enhanced after injection of contrast agent [15]. Lymphoma arising from skeleton generally manifests osteolytic damage at the femur, pelvis, spine and skull as well as surrounding masses, showing larger area of mass than osteolytic damage rarely with periosteal reaction [16,17]. The 3

cases reported in the present study are all found with extra-nodal tissues invasion at 8 different locations but no extra-nodal tissues invasion in the other case. Gastrointestinal invasion was not found in all 4 patients, probably due to the small sample size and mono histological type. Whether lymphadenopathy is resulted from extra-nodal tissue invasion of lymphoma still needs to be proved in further study.

The distinctive histological features of all 4 cases include: diffuse tumor cells with uniformly moderate size, karyokinesis and starry-sky sign. Immunohistochemically, LCA, CD10, CD20, Bcl-6 and Ki-67 are found positive in almost all the cases of lymphoma. The positive rate of Ki67 is almost 100% and therefore has significance in clinical diagnosis. The cell morphology and immunohistochemical findings of the 4 cases are in agreement to the diagnostic criteria for Burkitt lymphoma.

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